

Moving rehabilitation research forward: Developing consensus statements for rehabilitation and recovery research

Bernhardt, Julie; Borschmann, Karen; Boyd, Lara; Carmichael, S. Thomas; Corbett, Dale; Cramer, Steven C.; Hoffmann, Tammy; Kwakkel, Gert; Savitz, Sean I.; Saposnik, Gustavo; Walker, Marion; Ward, Nick

Published in:
Neurorehabilitation and Neural Repair

DOI:
[10.1177/1545968317724290](https://doi.org/10.1177/1545968317724290)

Licence:
Other

[Link to output in Bond University research repository.](#)

Recommended citation(APA):
Bernhardt, J., Borschmann, K., Boyd, L., Carmichael, S. T., Corbett, D., Cramer, S. C., Hoffmann, T., Kwakkel, G., Savitz, S. I., Saposnik, G., Walker, M., & Ward, N. (2017). Moving rehabilitation research forward: Developing consensus statements for rehabilitation and recovery research. *Neurorehabilitation and Neural Repair*, 31(8), 694-698. <https://doi.org/10.1177/1545968317724290>

General rights

Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

For more information, or if you believe that this document breaches copyright, please contact the Bond University research repository coordinator.

Moving rehabilitation research forward: developing consensus statements for rehabilitation and recovery research.

Julie Bernhardt ^{1,2}

Karen Borschmann ^{1,2}

Lara Boyd³

S Thomas Carmichael⁴

Dale Corbett^{5,6}

Steven C Cramer⁷

Tammy Hoffmann⁸

Gert Kwakkel⁹

Sean Savitz¹⁰

Gustavo Saposnik¹¹

Marion Walker¹²

Nick Ward^{13, 14}

¹Centre for Research Excellence in Stroke Rehabilitation and Recovery, Australia

²The Florey Institute of Neuroscience and Mental Health, Melbourne, Australia

³Department of Physical Therapy and the Djavad Mowafaghian Centre for Brain Health, University of British Columbia, Canada

⁴Departments of Neurology and Neurobiology, David Geffen School of Medicine at UCLA, United States

⁵Department of Cellular and Molecular Medicine, University of Ottawa, Canada

⁶Canadian Partnership for Stroke Recovery, University of Ottawa, Canada

⁷Depts. Neurology, Anatomy & Neurobiology, and Physical Medicine & Rehabilitation, University of California, Irvine, USA

⁸Centre for Research in Evidence-Based Practice, Bond University, Robina, Queensland, Australia

⁹Department of Rehabilitation Medicine, Neuroscience Campus Amsterdam, VU University Medical Centre, Amsterdam, The Netherlands

¹⁰Department of Neurology, McGovern Medical School, UT Health, Houston, Texas, United States

¹¹Department of Medicine, University of Toronto, Canada

¹²Division of Rehabilitation and Ageing, University of Nottingham, Nottingham, United Kingdom

¹³Sobell Department of Motor Neuroscience UCL Institute of Neurology, Queen Square, London, United Kingdom

¹⁴National Hospital for Neurology and Neurosurgery, Queen Square, London, United Kingdom

Word count: 1749

Keywords: consensus, neuro-biology, recovery, rehabilitation, recommendations, stroke

ABSTRACT

Stroke recovery is the next frontier in stroke medicine. While growth in rehabilitation and recovery research is exponential, a number of barriers hamper our ability to rapidly progress the field. Standardised terminology is absent in both animal and human research, methods are poorly described, recovery biomarkers are not well defined and we lack consistent timeframes or measures to examine outcomes. Agreed methods and conventions for developing, monitoring, evaluating and reporting interventions directed at improving recovery are lacking, and current approaches are often not underpinned by biology. We urgently need to better understand the biology of recovery and its time course in both animals and humans to translate evidence from basic science into clinical trials. A new international partnership of stroke recovery and rehabilitation experts has committed to advancing the research agenda. In May 2016 the first Stroke Recovery and Rehabilitation Roundtable will be held, with the aim of achieving an agreed approach to the development, conduct and reporting of research. A range of methods will be used to achieve consensus in four priority areas: Pre-clinical recovery research; Biomarkers of recovery; Intervention development, monitoring and reporting and; Measurement in clinical trials. We hope to foster a global network of researchers committed to advancing this exciting field. Recovery from stroke is challenging for many survivors. They deserve effective treatments underpinned by our evolving understanding of brain recovery and human behaviour. Working together we can develop game-changing interventions to improve recovery and quality of life in those living with stroke.

Introduction: The problem and solution

The explosion of knowledge about the stroke-damaged brain must be incorporated into our collective thinking about the nature and delivery of rehabilitation and restorative therapies (1). Variable methodological quality of animal studies (2), poorly defined interventions (3), and lack of agreed methods for developing, monitoring, evaluating and reporting interventions limit translation of research into evidence-based therapies (4). Furthermore, patient descriptions are not standardised, recovery biomarkers are not well defined (5) and we lack agreed time-points or measures to examine outcomes in rehabilitation and recovery trials (6).

By creating an international partnership of experts from a broad range of scientific and clinical disciplines, we aim to achieve consensus on developing, conducting and reporting rehabilitation and recovery research, and create a new community of practice. In this first roundtable, four areas we will examine represent important roadblocks to current research efforts. The aim of this paper is to summarise priorities for each theme.

Theme 1: Pre-clinical recovery research: 'Addressing the first translational gap'

To address the first gap in translation, we need to better translate pre-clinical evidence into human discovery trials in a bidirectional and iterative manner. The goal is to develop a deeper understanding of the neurobiology of recovery in human stroke survivors. Basic scientists need to understand the most pressing issues in stroke recovery and rehabilitation and work closely with their clinical counterparts in designing studies, taking a "Bedside to Bench" approach instead of the conventional "Bench to Bedside" approach. Understanding the biology and timing of recovery in animals and in humans requires knowledge of underlying molecular mechanisms that may be influenced by different therapies, such as rehabilitation and stem cells (5), with the potential to augment post-stroke plasticity and brain repair. Methods for enhancing the potential for functional and structural plasticity in surviving brain and spinal cord are needed (7-9). Translation will improve by defining inter-species differences, developing robust, pre-clinical animal models that better represent clinical stroke populations (older, with co-morbidities) (10) who do not recover within a few weeks post-stroke (11), and identifying more reliable, valid and sensitive histological and

behavioural outcomes (7). Another important issue is to hold pre-clinical studies to the same quality standards and rigor as clinical research (12). Sample size, age groups, and gender differences are not often considered in pre-clinical studies, ultimately limiting their clinical translation (2, 13, 14). Thus, a main point of pre-clinical studies of stroke repair is to model human recovery.

Theme 2: Recovery biomarkers

A key impediment to the development of new therapies for promoting recovery after stroke is not knowing who or when best to treat. One of the most important findings to emerge from decades of work in rodents was the identification of a period of spontaneous biological recovery during which the effect of training is heightened (15). Investigating the mechanisms involved in humans would reveal exciting therapeutic targets. A different type of problem, specific to human studies, is heterogeneity in the residual structural and functional post-stroke brain architecture and the impact this has on potential interventions (16, 17). The answer to ‘who and when’ is the development of biomarkers to provide knowledge of both therapeutic targets and prognosis in human stroke. There are limited validated biological markers of stroke recovery, but promising potential targets exist (5). We define stroke recovery biomarkers as “indicators of disease state that can be used clinically to reflect underlying molecular/cellular events and/or predict outcome associated with recovery from stroke”, which may include markers of biology (blood, genetics), imaging (structural, functional, chemical), neurophysiology (patterns of brain excitability or electrical activity), or combinations of such (1, 18, 19). While most research has explored relationships between late biomarkers (3-6 months post-stroke) and final stages of recovery (19, 20), investigation of early biomarkers (<7 days) reflecting the mechanisms of spontaneous biological recovery is an urgent priority. Furthermore, distinction is required between cross-sectional measures that capture biological state, measures that predict future clinical events, and measures that change in parallel with behavioural change; each of these has value in stroke research.

Blood biomarker analysis is viable because many brain-derived molecules cross the blood-brain-barrier, including micro-RNA's, lipids, short peptide chains, and exosomes. Based on

similar analyses from traumatic brain injury (21) and Alzheimer's Disease (22), there is an expectation of identifying molecular signatures of recovery post-stroke in humans (23). Individuals' genetic profiles may also influence recovery (24-26). While interest has centred on genes known to contribute to neuroplasticity (27), there are a number of candidate biomarkers to consider as well as gene-gene interactions, and epigenetics.

Considerable attention has focused on brain imaging to define post-stroke patterns of recovery. Imaging is non-invasive and easily accessible, enabling categorisation of brain anatomy, function, chemistry and connectivity (28-31). Another potential recovery biomarker is neurophysiological status, mapped using non-invasive brain stimulation (i.e., transcranial magnetic stimulation; TMS) (19, 30). TMS based neurophysiological measures of the electrophysiological relationship(s) between the cortical hemispheres (32) and corticospinal tract integrity via the generation of motor evoked potentials relate to motor outcome in chronic (19, 33) and acute stroke (34). However their value in predicting recovery is not well understood.

Recovery biomarker use may foster developments in new therapies and improve clinical trial efficiency through better patient selection or stratification. Tailoring of therapies for individual patients based on their capacity for neural reorganisation and recovery will facilitate personalised interventions, guiding the delivery of effective treatment to the right people, at the right time. Once identified, we must define the psychometric qualities and performance of proposed biomarkers at different time-points of recovery. Prediction models for patient subgroups would need to be validated; this would require large cohorts and the development of a world-wide network (35).

Theme 3: Intervention development, monitoring and reporting

Sequential development, testing and refining of interventions through trial phasing is less common in stroke rehabilitation than other areas of stroke medicine. Furthermore, the description of interventions in stroke rehabilitation studies is typically incomplete and monitoring of interventions poorly described and reported (36), leading to significant research waste (3).

The need for systematic development of complex interventions has been highlighted for some time and useful frameworks exist (37). To date, researchers employ various methods to develop interventions intended for evaluation; and many fail to describe the underpinning theoretical framework or intended biological mechanisms to improve recovery or outcomes. Dosing studies in the trial development phase are rare (38) and insufficient attention has been paid to how much training is needed, and when it should be applied to drive neurological recovery. Too often, our choice of intervention type, dose or scheduling is arbitrarily assigned (as reflected in many meta-analyses of stroke rehabilitation interventions), with a 'more is better' mantra that is likely too simplistic and may even be harmful at certain points in the recovery pathway (39). In complex behaviour change research, we see increased attention on co-design of interventions with the health consumer (40); turning these types of interventions into standardised protocols for delivery in trials is not simple.

Intervention fidelity is also poorly addressed in most rehabilitation trials, with few reporting the methods used to monitor the delivery of interventions. While interest in the area is growing (41-43), establishing agreed standards for monitoring and reporting of fidelity would significantly improve our research. When evidence of intervention efficacy exists, insufficient reporting of intervention protocol is a substantial barrier to reliable implementation or replication of research findings, yet this has received little attention (3). The Template for Intervention Description and Replication (TIDieR), which provides authors with guidance about how to structure accounts of their interventions (44) is a step in the right direction. But we must improve how we develop, monitor and report interventions. This will reduce research waste and, when interventions are effective, hasten translation into clinical practice.

Theme 4: Measurement in clinical trials

The number of rehabilitation trials is growing exponentially, however many (98% of physical therapy trials in one recent review) (45) are underpowered, single site, testing feasibility of an intervention or are proof-of-concept trials. Systematic reviews of rehabilitation trials are challenging given the high variability in outcomes used, the timing of intervention delivery

and outcome assessment (6). These problems are further compounded by poor reporting of interventions raised in Theme 3. If researchers used a core set of trial measures, gathered at agreed time-points after stroke, our ability to compare results across trials, pool data for meta-analyses or undertake individual patient meta-analyses would be vastly improved. Large pooled data sets from rehabilitation trials could be used to develop hypotheses about stroke recovery or help validate prognostic tools. We also need to consider how we stratify patients in trials and whether recovery biomarkers are robust enough for that purpose (Theme 2). When recruitment occurs later after stroke, some measure of stroke severity at time of onset is critical to developing our understanding of recovery. We may need to consider new recruitment models that track patients from stroke onset, or retrospectively acquiring reliable and simple proxy measures of baseline severity. Insufficient attention has also been paid to systematic acquisition of pre-stroke lifestyle and other variable that are likely to inform stroke recovery phenotypes.

Limitations of many measurement tools are well known and a number of frameworks exist to support selection of core measurements, for example the international classification of functioning, disability and health (ICF) model, and COSMIN (www.cosmin.nl) which provides criteria for evaluating psychometric properties of tools. Importantly, we need to ensure that tools we adopt can measure meaningful change and can distinguish true neurological repair from use of adaptation strategies to achieve a goal (46). Important achievements would be to standardise definitions for common terms (eg recovery), time-points of measurement and distinguish between different types of outcomes (47). Simply stated, our challenge is not just to agree a core set of measurements, but to consider what we need to measure and why, to improve rehabilitation and recovery trial methods (48, 49).

CONCLUSION

A new partnership of around 60 leading stroke experts has committed to advancing stroke recovery and rehabilitation, by achieving an agreed approach on how to develop, conduct and report research across the four reported themes. A key issue to address is defining important time-points in stroke recovery, underpinned by our best understanding of biological processes. The next step towards developing consensus is the inaugural Stroke Recovery and Rehabilitation Roundtable meeting, to be held in Philadelphia, USA, in May 2016. Recommendations from this meeting will be pivotal for progressing stroke recovery and rehabilitation research, and provide impetus for development of strong international partnerships to tackle the challenge of improving stroke recovery.

REFERENCES

1. Hachinski V, Donnan GA, Gorelick PB, Hacke W, Cramer SC, Kaste M, et al. Stroke: working toward a prioritized world agenda. *International Journal of stroke*. 2010;5(4):238-56.
2. Fisher M, Feuerstein G, Howells DW, Hurn PD, Kent TA, Savitz SI, et al. Update of the stroke therapy academic industry roundtable preclinical recommendations. *Stroke*. 2009;40(6):2244-50. Epub 2009/02/28.
3. Hoffmann TC, Walker MF. 'TIDieR-ing up' the reporting of interventions in stroke research: the importance of knowing what is in the 'black box'. *International Journal of Stroke*. 2015;10(5):657-8.
4. Walker MF, Fisher RJ, Korner-Bitensky N, McCluskey A, Carey LM. From what we know to what we do: translating stroke rehabilitation research into practice. *International journal of stroke : official journal of the International Stroke Society*. 2013;8(1):11-7. Epub 2013/01/03.
5. Savitz SI, Cramer SC, Wechsler L. Stem cells as an emerging paradigm in stroke 3: enhancing the development of clinical trials. *Stroke*. 2014;45(2):634-9. Epub 2013/12/26.
6. Ali M, English C, Bernhardt J, Sunnerhagen KS, Brady M, Collaboration VI-R. More outcomes than trials: a call for consistent data collection across stroke rehabilitation trials. *International Journal of stroke*. 2013;8(1):18-24.
7. Murphy TH, Corbett D. Plasticity during stroke recovery: from synapse to behaviour. *Nature reviews Neuroscience*. 2009;10(12):861-72. Epub 2009/11/06.
8. Carmichael ST. Emergent properties of neural repair: elemental biology to therapeutic concepts. *Annal Neurol*. 2016;In press.
9. Carmichael ST. Brain excitability in stroke: the yin and yang of stroke progression. *Arch Neurol*. 2012;69(2):161-7. Epub 2011/10/12.
10. Carmichael ST. Rodent models of focal stroke: size, mechanism, and purpose. *NeuroRx : the journal of the American Society for Experimental NeuroTherapeutics*. 2005;2(3):396-409. Epub 2006/01/04.
11. Corbett D, Jeffers M, Nguemeni C, Gomez-Smith M, Livingston-Thomas J. Lost in translation: rethinking approaches to stroke recovery. *Progress in Brain Research*. 2015;218:413- 34.

12. O'Collins VE, Macleod MR, Donnan GA, Horky LL, van der Worp BH, Howells DW. 1,026 experimental treatments in acute stroke. *Annals of neurology*. 2006;59(3):467-77. Epub 2006/02/03.
13. Dirnagl U. Bench to bedside: the quest for quality in experimental stroke research. *Journal of Cerebral Blood Flow & Metabolism*. 2006;26(12):1465-78.
14. Kimmelman J, Mogil JS, Dirnagl U. Distinguishing between exploratory and confirmatory preclinical research will improve translation. *PLoS Biol*. 2014;12(5):e1001863.
15. Zeiler SR, Krakauer JW. The interaction between training and plasticity in the poststroke brain. *Curr Opin Neurol*. 2013;26(6):609-16. Epub 2013/10/19.
16. Burke E, Cramer SC. Biomarkers and predictors of restorative therapy effects after stroke. *Current neurology and neuroscience reports*. 2013;13(2):329. Epub 2013/01/10.
17. Wadden KP, Woodward TS, Metzrak PD, Lavigne KM, Lakhani B, Auriat AM, et al. Compensatory motor network connectivity is associated with motor sequence learning after subcortical stroke. *Behavioural Brain Research*. 2015;286:136-45.
18. Di Luca M, Baker M, Corradetti R, Kettenmann H, Mendlewicz J, Olesen J, et al. Consensus Document on European Brain Research. *European Journal of Neuroscience*. 2011;33:768-818.
19. Mang CS, Borich MR, Brodie SM, Brown KE, Snow NJ, Wadden KP, et al. Diffusion imaging and transcranial magnetic stimulation assessment of transcallosal pathways in chronic stroke. *Clinical neurophysiology : official journal of the International Federation of Clinical Neurophysiology*. 2015;126(10):1959-71. Epub 2015/01/30.
20. Borich MR, Mackay AL, Vavasour IM, Rauscher A, Boyd LA. Evaluation of white matter myelin water fraction in chronic stroke. *NeuroImage Clinical*. 2013;2:569-80. Epub 2013/11/02.
21. Diaz-Arrastia R, Wang KK, Papa L, Sorani MD, Yue JK, Puccio AM, et al. Acute biomarkers of traumatic brain injury: relationship between plasma levels of ubiquitin C-terminal hydrolase-L1 and glial fibrillary acidic protein. *Journal of neurotrauma*. 2014;31(1):19-25. Epub 2013/07/20.
22. Fiandaca MS, Mapstone ME, Cheema AK, Federoff HJ. The critical need for defining preclinical biomarkers in Alzheimer's disease. *Alzheimer's & dementia : the journal of the Alzheimer's Association*. 2014;10(3 Suppl):S196-212. Epub 2014/06/14.
23. Dromerick AW, Edwardson MA, Edwards DF, Giannetti ML, Barth J, Brady KP, et al. Critical periods after stroke study: translating animal stroke recovery experiments into a clinical trial. *Frontiers in human neuroscience*. 2015;9.
24. Pearson-Fuhrhop K, Burke E, Cramer S. The influence of genetic factors on brain plasticity and recovery after neural injury. *Current opinion in neurology*. 2012;25(6):682-8.
25. Mang CS, Campbell KL, Ross CJ, Boyd LA. Promoting neuroplasticity for motor rehabilitation after stroke: considering the effects of aerobic exercise and genetic variation on brain-derived neurotrophic factor. *Phys Ther*. 2013;93(12):1707-16. Epub 2013/08/03.
26. Carey LM, Crewther S, Salvado O, Linden T, Connelly A, Wilson W, et al. STroke imAging pRevention and treatment (START): A longitudinal stroke cohort study: Clinical trials protocol. *International journal of stroke : official journal of the International Stroke Society*. 2015;10(4):636-44. Epub 2013/11/12.
27. Di Lazzaro V, Pellegrino G, Di Pino G, Corbetta M, Ranieri F, Brunelli N, et al. Val66Met BDNF gene polymorphism influences human motor cortex plasticity in acute stroke. *Brain stimulation*. 2015;8(1):92-6. Epub 2014/09/23.
28. Burke E, Dobkin BH, Noser EA, Enney LA, Cramer SC. Predictors and biomarkers of treatment gains in a clinical stroke trial targeting the lower extremity. *Stroke*. 2014;45(8):2379-84. Epub 2014/07/30.
29. Corbetta M, Ramsey L, Callejas A, Baldassarre A, Hacker CD, Siegel JS, et al. Common behavioral clusters and subcortical anatomy in stroke. *Neuron*. 2015;85(5):927-41.
30. Stinear C, Barber P, Coxon J, Fleming M, Byblow W. Priming the motor system enhances the effects of upper limb therapy in chronic stroke. *Brain : a journal of neurology*. 2008;131(Pt 5):1381-90. Epub 2008/03/22.

31. Wu J, Quinlan EB, Dodakian L, McKenzie A, Kathuria N, Zhou RJ, et al. Connectivity measures are robust biomarkers of cortical function and plasticity after stroke. *Brain : a journal of neurology*. 2015;138(Pt 8):2359-69. Epub 2015/06/14.
32. Murase N, Duque J, Mazzocchio R, Cohen LG. Influence of interhemispheric interactions on motor function in chronic stroke. *Annals of neurology*. 2004;55(3):400-9. Epub 2004/03/03.
33. Stinear C, Barber P, Smale P, Coxon J, Fleming M, Byblow W. Functional potential in chronic stroke patients depends on corticospinal tract integrity. *Brain : a journal of neurology*. 2007;130(Pt 1):170-80. Epub 2006/12/07.
34. Stinear C, Barber P, Petoe M, Anwar S, Byblow W. The PREP algorithm predicts potential for upper limb recovery after stroke. *Brain : a journal of neurology*. 2012;135(Pt 8):2527-35. Epub 2012/06/13.
35. Kwakkel G, Kollen B. Predicting activities after stroke: what is clinically relevant? *International Journal of stroke*. 2013;8(1):25-32.
36. Hoffmann TC, Walker MF, Langhorne P, Eames S, Thomas E, Glasziou P. What's in a name? The challenge of describing interventions in systematic reviews: analysis of a random sample of reviews of non-pharmacological stroke interventions. *BMJ open*. 2015;5(11):e009051.
37. Craig P, Dieppe P, Macintyre S, Michie S, Nazareth I, Petticrew M. Developing and evaluating complex interventions: the new Medical Research Council guidance. *BMJ*. 2008;337:a1655. Epub 2008/10/01.
38. Dite W, Langford ZN, Cumming TB, Churilov L, Blennerhassett JM, Bernhardt J. A Phase 1 exercise dose escalation study for stroke survivors with impaired walking. *International journal of stroke : official journal of the International Stroke Society*. 2015;10(7):1051-6. Epub 2015/06/30.
39. Bernhardt J, Churilov L, Ellery F, Collier J, Chamberlain J, Langhorne P, et al. Prespecified dose-response analysis for A Very Early Rehabilitation Trial (AVERT). *Neurology*. 2016. Epub 2016/02/19.
40. Batalden M, Batalden P, Margolis P, Seid M, Armstrong G, Opipari-Arrigan L, et al. Coproduction of healthcare service. *BMJ quality & safety*. 2015. Epub 2015/09/18.
41. Poltawski L, Norris M, Dean S. Intervention fidelity: developing an experience-based model for rehabilitation research. *J Rehabil Med*. 2014;46(7):609-15. Epub 2014/06/19.
42. Masterson-Algar P, Burton CR, Rycroft-Malone J, Sackley CM, Walker MF. Towards a programme theory for fidelity in the evaluation of complex interventions. *J Eval Clin Pract*. 2014;20(4):445-52. Epub 2014/05/21.
43. Collier JM, Bernhardt J. The therapy 'pill': Achieving treatment dose within a rehabilitation trial. *Brain Impairment*. 2008;9(02):191-7.
44. Hoffmann TC, Glasziou PP, Boutron I, Milne R, Perera R, Moher D, et al. Better reporting of interventions: template for intervention description and replication (TIDieR) checklist and guide. *BMJ*. 2014;348:g1687. Epub 2014/03/13.
45. Veerbeek J, van Wegen E, van Peppen R, van der Wees P, Hendriks E, Rietberg M, et al. What is the evidence for physical therapy poststroke? A systematic review and meta-analysis. *PLoS ONE*. 2014;9(2):e87987.
46. Buma F, Kwakkel G, Ramsey N. Understanding upper limb recovery after stroke. *Restorative neurology and neuroscience*. 2013;31(6):707-22. Epub 2013/08/22.
47. Levin MF, Kleim JA, Wolf SL. What do motor "recovery" and "compensation" mean in patients following stroke? *Neurorehabil Neural Repair*. 2008.
48. Yozbatiran N, Der-Yeghiaian L, Cramer SC. A standardized approach to performing the action research arm test. *Neurorehabil Neural Repair*. 2008;22(1):78-90.
49. See J, Dodakian L, Chou C, Chan V, McKenzie A, Reinkensmeyer DJ, et al. A standardized approach to the Fugl-Meyer assessment and its implications for clinical trials. *Neurorehabil Neural Repair*. 2013;1545968313491000.